REMARKS

Status of the claims

Claims 1-28 are pending and currently under consideration in the present application. By virtue of this amendment, claims 23 and 24 have been amended and new claims 29 and 30 have been added.

The amendments and new claims are supported by the specification. An amendment was made to claim 23 was made to correct a typographical error by changing the word "methods" to "method." A cosmetic, non-narrowing amendment was made to claims 23 and 24 to amend "protein" to "test protein." Support for the amendments to claims 23 and 24 may be found, for example, in paragraph [0127]. Support for new claim 29 may be found, for example, in paragraph [0055]. Support for new claim 30 may be found, for example, in paragraph [0066].

With respect to any claim amendments or cancellations, Applicants have not dedicated to the public or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Rejection under 35 U.S.C. §112, second paragraph

Claim 24 has been rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Applicants respectfully traverse this rejection.

The Office Action states that claim 24 is vague and confusing because it recites "about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14" and is dependent upon claim 1, which recites "at least 15 digital antibodies." The Examiner alleges that claim 24 does not further limit claim 23. Office Action, page 2. In response, Applicants respectfully note that claim 1 recites a set of digital antibodies comprising at least about 15 digital antibodies, whereas claim 24 as amended recites that "at least about 7 . . . digital antibodies *bind the test protein*" (emphasis added). Claim 24 is dependent upon claim 23, which recites a method for identifying a test protein

comprising, *inter alia*, contacting a sample comprising the test protein with the set of digital antibodies according to claim 1 under conditions that permit binding, wherein at least about six digital antibodies bind the test protein. Thus, claim 24 as amended recites a method wherein a sample is contacted with a set of digital antibodies comprising at least about 15 digital antibodies (in accordance with claim 1), wherein at least about 7 of the digital antibodies in the set bind the test protein.

Claim 24 further limits claim 23, which recites that at least about six digital antibodies bind the test protein. Claim 24 recites that at least about 7 digital antibodies bind the test protein and thus provides a further limitation with respect to the at least about six digital antibodies recited to bind the test protein in claim 23.

Claim 24 also is not indefinite by virtue of its dependence on claim 1, because claim 1 does not recite that any of the digital antibodies in the claimed antibody set bind a test protein, whereas claim 24 recites that at least about 7 of the digital antibodies in the set bind a test protein.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §102(b)

Claims 1, 9-11, 12, 14, 16-26, and 28 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Belov et al. (2001) *Cancer Research* 61:4483. Applicants respectfully traverse this rejection.

Belov et al. teach an antibody microarray that contains 60 different antibodies that each binds *specifically* to a particular cell surface marker. In contrast the currently claimed digital antibodies recognize very small epitopes, and are expected to bind to multiple proteins in a sample. As discussed in the specification, "[t]he present invention stems from the insight that cross-reactive antibodies (i.e., antibodies that recognize small epitopes, and thus are expected to bind a multiplicity of proteins) may be used in combination to generate a protein binding profile of sufficient specificity such that samples may be characterized, uniquely identified (including identification of

one or more components in a sample) and/or distinguished. Thus, *specificity of results and information arising from antibody binding is conferred via the binding of sets of digital antibodies to protein in a sample (whereby a specific protein binding profile is generated), rather than by binding of a single antibody that binds but one or a few proteins, as commonly used in the art for specific detection.*" Paragraph [0053], emphasis added. Belov et al. teach a microarray comprised of antibodies that each specifically bind to a particular cell surface antigen. In contrast, the present claims are directed to a *set* of antibodies, each binding to a small epitope of 3-5 amino acids rather than to a particular protein. Short 3-5 amino acid sequences may be found in multiple proteins. For example, a review of Georgetown University's Non-Redundant Reference Protein Database (release 1.48, June 28, 2004, containing 1,635,630 entries, accessible at http://pir.georgetown.edu/pirwww/search/pirnref.shtml) reveals that the 3 amino acid sequence DTG is found in 98,464 proteins, the 4 amino acid sequence KTTN is found in 3,888 proteins, the amino acid sequence TGKXE (where X indicates any amino acid) is found in 7,299 proteins, and the 5 amino acid sequence TGKLL is found in 1,030 proteins. Therefore, a small epitope recognized by the claimed digital antibodies may be present on many proteins in a sample, and detection or identification of a protein of interest may result from a characteristic pattern generated by binding of a *plurality* of digital antibodies to the protein rather than via specific binding of a single antibody as taught in Belov et al. Thus, Belov et al., which discloses a microarray of antibodies each capable of binding a specific protein, does not anticipate the presently claimed invention.

The Examiner states that it is an inherent characteristic that epitopes recognized by antibodies usually consist of at least 3, 4, or more consecutive amino acids. Office Action, page 3. Applicants respectfully disagree with this statement. As an initial matter, Applicants respectfully note that none of the claims recites an epitope consisting of *at least* 3, 4, or more amino acids, as asserted by the Examiner. Rather, claim 1 recites an epitope consisting of 3 or 4 amino acids, and an epitope consisting of 5 consecutive amino acids is recited in some dependent claims. Therefore, the epitopes recognized by the digital antibodies of the invention are limited to 3-5 amino acids. Antibodies that specifically bind to protein antigens have been shown to bind a unique conformational epitopes or a long linear epitopes consisting of 8-12 amino acids. (Saul and Alzari

(1996) "Crystallographic Studies of Antigen-Antibody Interactions" in *Epitope Mapping Protocols*, G.E. Morris, ed., Humana Press, Totowa, NJ. A copy of this reference is provided in a Supplemental Information Disclosure Statement, submitted concurrently herewith.) Therefore, binding to an epitope that *consists of* 3, 4, or 5 amino acids, as presently claimed, is not an inherent property of classical antibodies that are capable of specific binding to a protein antigen.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b).

Rejection under 35 U.S.C. §102(e)

Claims 1-28 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by Chait et al., U.S. Patent Application No. 2003/0045694. Applicants respectfully traverse this rejection.

Chait et al. teach compositions and methods for analyte detection. In one embodiment, referred to by the Examiner, a microarray containing 3200 immobilized antibodies is used for binding and immobilization of protein molecules to which a DNA tag has been attached, followed by addition of a PNA-peptide reporter molecule and signal detection. The Examiner states that Chait et al. teach a microarray with 3200 antibodies which would inherently encompass less antibodies, such as 100, 200, 300, . . .1000 antibodies as recited in claim 5. However, Applicants respectfully maintain that Chait et al. do not teach *digital antibodies that bind small epitopes of 3-5 amino acids* as presently claimed. As discussed above and as disclosed in the present specification, antibodies that bind small epitopes as claimed are expected to each bind to a number of proteins in a sample, *i.e.*, they are cross-reactive with multiple proteins. Chait et al. do not teach such antibodies, or use of such antibodies in their disclosed array.

The Examiner also states that Chait et al. also teach pretreatment of test samples by digestion or enzymatic cleavage, removal of unbound protein, collection of protein binding profile data, and that test samples may be peptides, proteins, cell, or viruses. In response, Applicants respectfully maintain that Chait et al. do not teach the use of digital antibodies that bind small

epitopes of 3-5 amino acids in any of these embodiments. Therefore, this reference does not anticipate Applicants' claimed invention.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e).

Rejection under 35 U.S.C. §103(a)

Claims 2-8 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Belov et al. in view of Chait et al. Applicants respectfully traverse this rejection.

A *prima facie* case for obviousness includes, *inter alia*, a requirement that references, when combined, must teach or suggest all the limitations of a claimed invention. MPEP § 2142. Belov et al., in combination with Chait et al., do not teach or suggest all of the limitations of the present invention as claimed. As discussed above, Belov et al. do not teach a set of digital antibodies that each binds an epitope consisting of 3-5 amino acids. Chait et al. do not supply this missing element. Chait et al. teach a microarray containing 3200 antibodies but do not teach antibodies that bind small epitopes of 3-5 amino acids as claimed. Thus, the combination of Belov et al. and Chait et al. does not render the claimed invention obvious.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **559312000100**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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